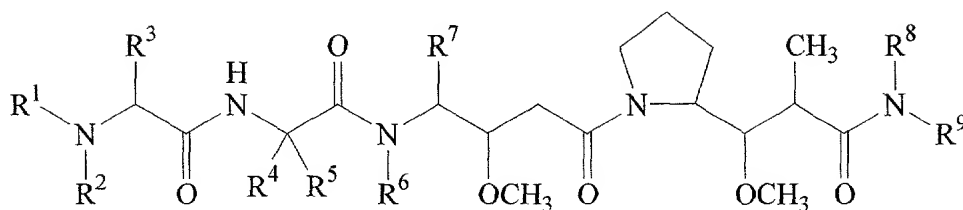


# CLAIMS

1. A compound of the formula



wherein, independently at each location:

R<sup>1</sup> is selected from hydrogen and lower alkyl;

R<sup>2</sup> is selected from hydrogen and lower alkyl;

R<sup>3</sup> is lower alkyl;

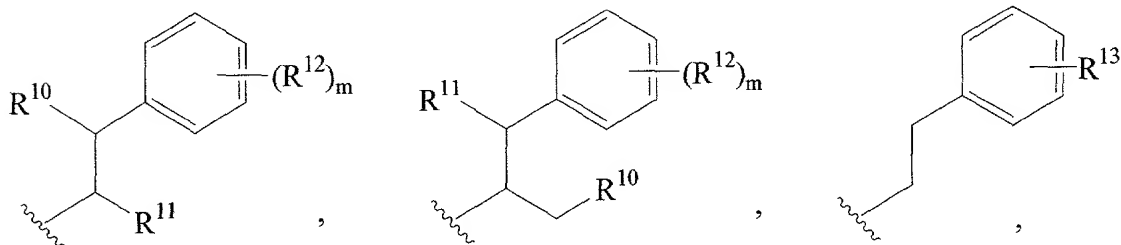
R<sup>4</sup> is selected from lower alkyl, aryl, and -CH<sub>2</sub>-C<sub>5-7</sub>carbocycle when R<sup>5</sup> is selected from H and methyl, or R<sup>4</sup> and R<sup>5</sup> together form a carbocycle of the partial formula -(CR<sup>a</sup>R<sup>b</sup>)<sub>n</sub>- wherein R<sup>a</sup> and R<sup>b</sup> are independently selected from hydrogen and lower alkyl and n is selected from 2, 3, 4, 5 and 6;

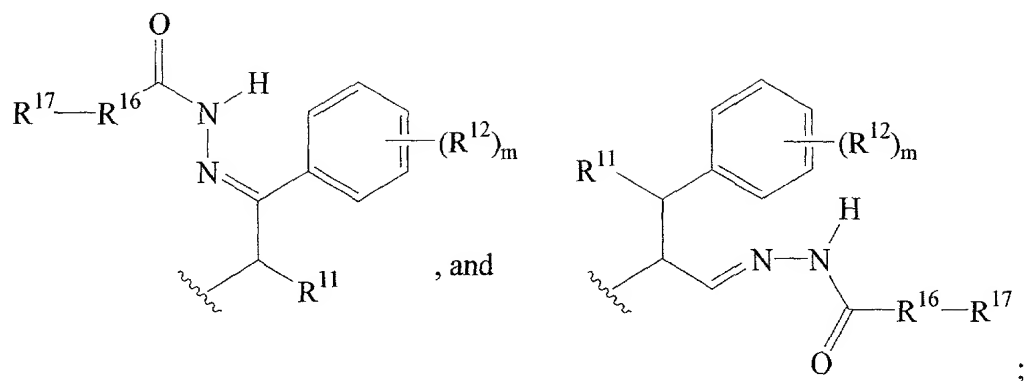
R<sup>6</sup> is selected from hydrogen and lower alkyl;

R<sup>7</sup> is *sec*-butyl or *iso*-butyl;

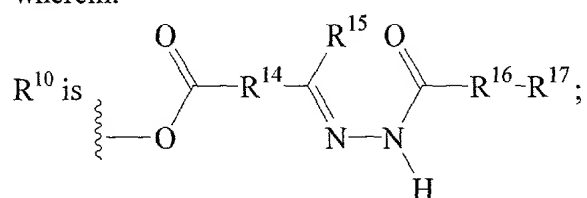
R<sup>8</sup> is selected from hydrogen and lower alkyl; and

R<sup>9</sup> is selected from





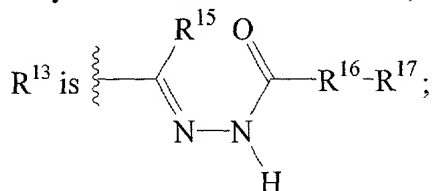
wherein:



$R^{11}$  is selected from hydrogen and lower alkyl;

$R^{12}$  is selected from lower alkyl, halogen, and methoxy, and  $m$  is 0-5

where  $R^{12}$  is independently selected at each occurrence; and

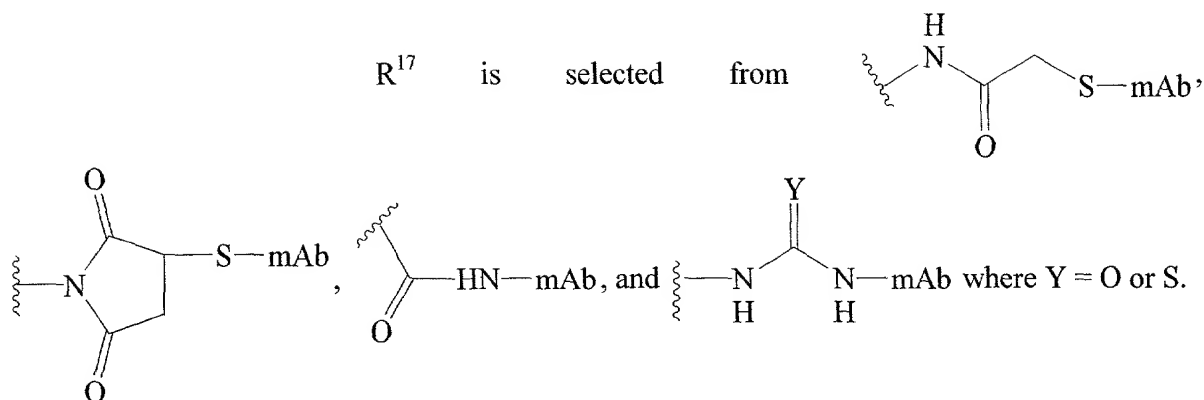


wherein:

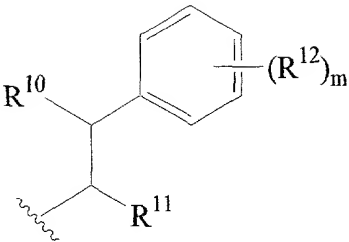
$R^{14}$  is selected from a direct bond, divalent lower alkyl and divalent aryl;

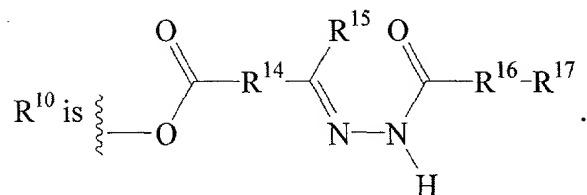
$R^{15}$  is selected from hydrogen, lower alkyl and aryl;

$R^{16}$  is selected from divalent lower alkyl, divalent aryl, and  $-(CH_2OCH_2)_pCH_2-$  where  $p$  is 1-5; and

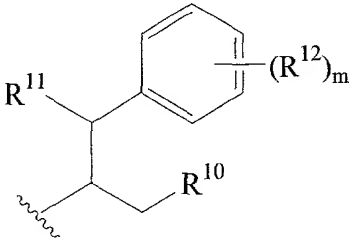


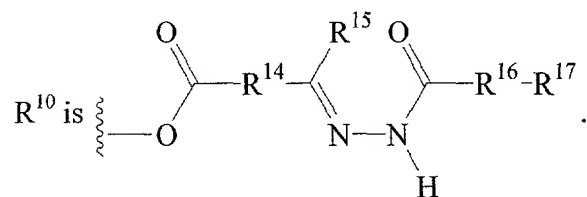
2. A compound of claim 1 wherein  $R^1$  is hydrogen.
3. A compound of claim 1 wherein  $R^1$  and  $R^2$  are methyl.
4. A compound of claim 1 wherein  $R^3$  is isopropyl.
5. A compound of claim 1 wherein  $R^4$  is selected from lower alkyl, aryl, and  $-\text{CH}_2-\text{C}_{5-7}\text{carbocycle}$  and  $R^5$  is selected from H and methyl.
6. A compound of claim 1 wherein  $R^4$  is selected from lower alkyl, and  $R^5$  is selected from H and methyl.
7. A compound of claim 1 wherein  $R^4$  and  $R^5$  together form a carbocycle of the partial formula  $-(\text{CR}^a\text{R}^b)_n-$  wherein  $R^a$  and  $R^b$  are independently selected from hydrogen and lower alkyl and  $n$  is selected from 2, 3, 4, 5 and 6.
8. A compound of claim 1 wherein  $R^6$  is lower alkyl.
9. A compound of claim 1 wherein  $R^8$  is hydrogen.

10. A compound of claim 1 wherein R<sup>9</sup> is  and



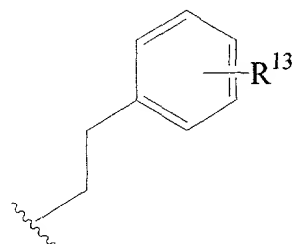
11. A compound of claim 10 wherein R<sup>14</sup> is selected from divalent aryl and divalent alkyl; R<sup>15</sup> is selected from lower alkyl and aryl; and R<sup>16</sup> is divalent lower alkyl.

12. A compound of claim 1 wherein R<sup>9</sup> is  and

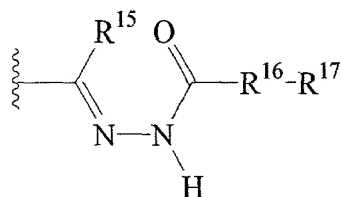


13. A compound of claim 12 wherein R<sup>14</sup> is selected from divalent aryl and divalent lower alkyl; R<sup>15</sup> is selected from lower alkyl and aryl; and R<sup>16</sup> is divalent lower alkyl.

14. A compound of claim 1 wherein R<sup>9</sup> is

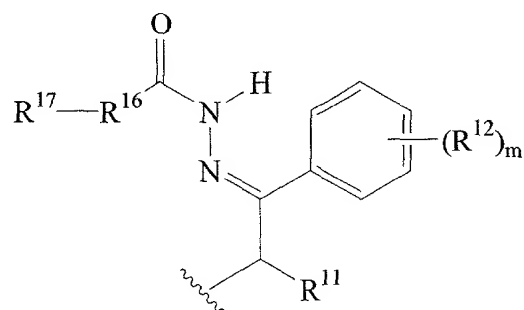


and R<sup>13</sup> is



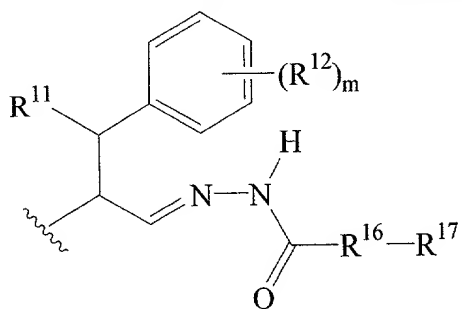
15. A compound of claim 14 wherein R<sup>15</sup> is lower alkyl; and R<sup>16</sup> is divalent lower alkyl.

16. A compound of claim 1 wherein R<sup>9</sup> is

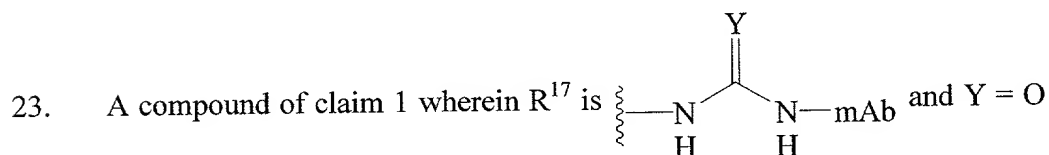
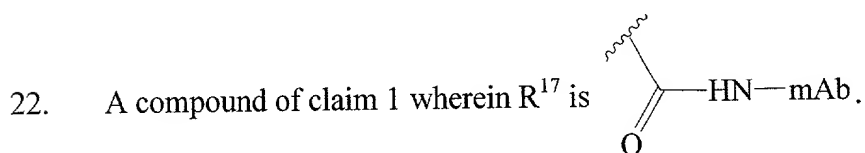
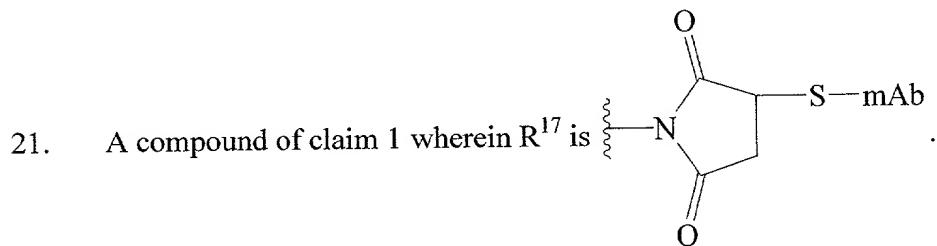
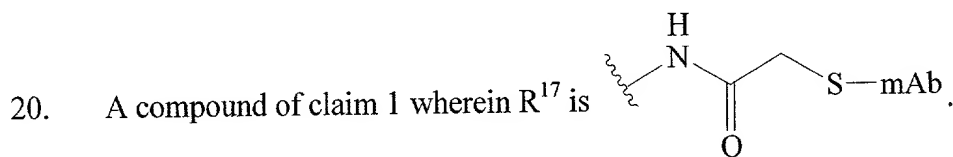


17. A compound of claim 16 wherein R<sup>16</sup> is selected from divalent lower alkyl and divalent aryl.

18. A compound of claim 1 wherein  $R^9$  is

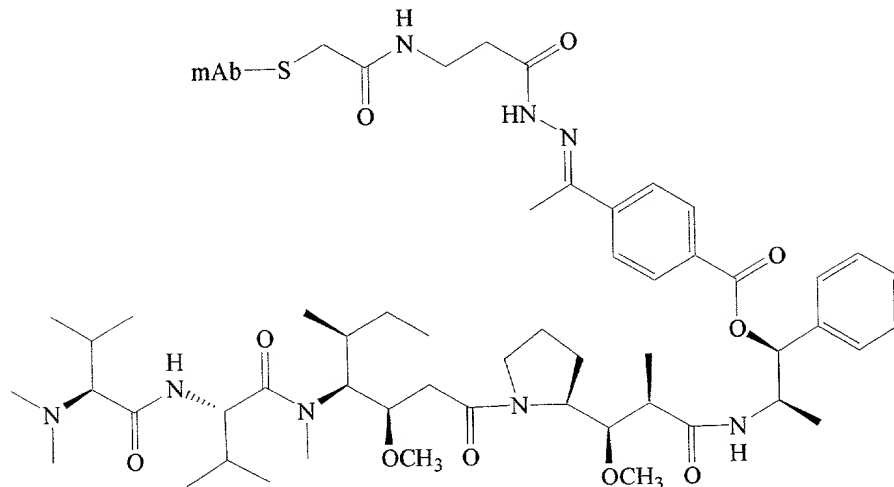


19. A compound of claim 18 wherein  $R^{16}$  is selected from divalent lower alkyl and divalent aryl.

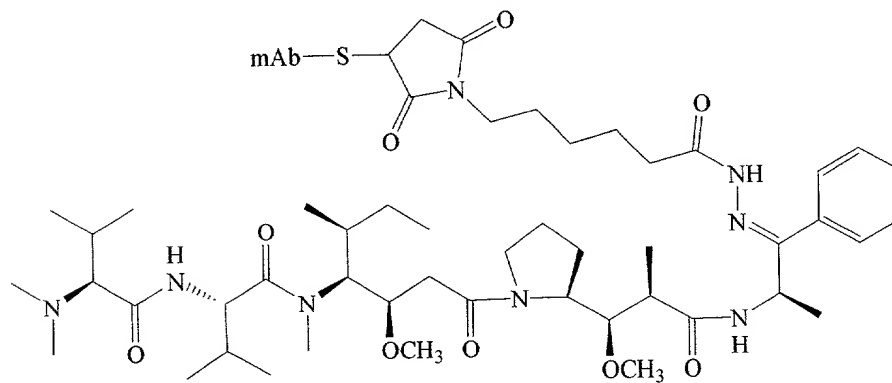


or S.

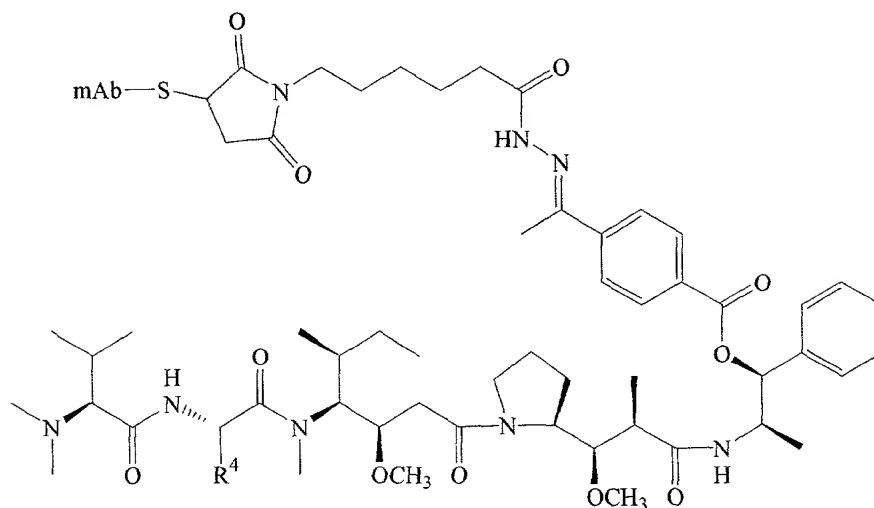
24. A compound of claim 1 having the structure



25. A compound of claim 1 having the structure

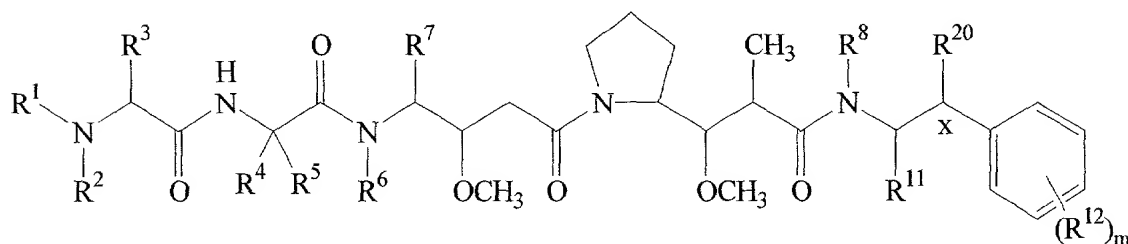


26. A compound of claim 1 having the structure



wherein  $R^4$  is selected from *iso*-propyl and *sec*-butyl.

27. A compound of the formula



wherein, independently at each location:

$R^2$  is selected from hydrogen and lower alkyl;

$R^3$  is lower alkyl;

$R^4$  is selected from lower alkyl, aryl, and  $-CH_2-C_{5-7}$ carbocycle when  $R^5$  is selected from H and methyl, or  $R^4$  and  $R^5$  together form a carbocycle of the partial formula  $-(CR^aR^b)_n-$  wherein  $R^a$  and  $R^b$  are independently selected from hydrogen and lower alkyl and n is selected from 2, 3, 4, 5 and 6;

$R^6$  is selected from hydrogen and lower alkyl;

$R^7$  is *sec*-butyl or *iso*-butyl;

$R^8$  is selected from hydrogen and lower alkyl;



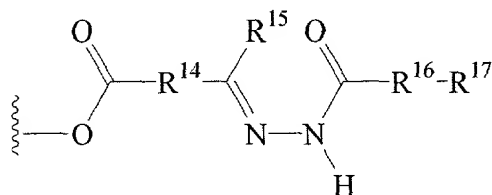
$R^{11}$  is selected from hydrogen and lower alkyl;

$R^{12}$  is selected from lower alkyl, halogen, and methoxy, and  $m$  is 0-5 where  $R^{12}$  is independently selected at each occurrence; and

$R^{20}$  is a reactive linker group having a reactive site that allows  $R^{20}$  to be reacted with a targeting moiety, where  $R^{20}$  can be bonded to the carbon labeled "x" by either a single or double bond.

28. A compound of claim 27 wherein the reactive site is selected from *N*-hydroxysuccinimide ester, *p*-nitrophenyl ester, pentafluorophenyl ester, isothiocyanate, isocyanate, anhydride, acid chloride, and sulfonyl chloride.

29. A compound of claim 27 wherein  $R^{20}$  comprises a hydrazone of the formula

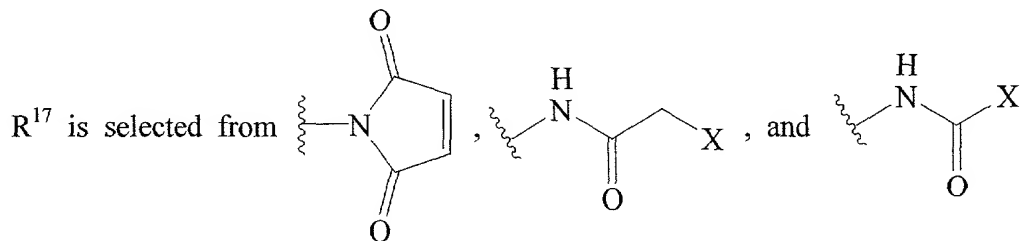


wherein:

$R^{14}$  is selected from a direct bond, divalent lower alkyl and divalent aryl;

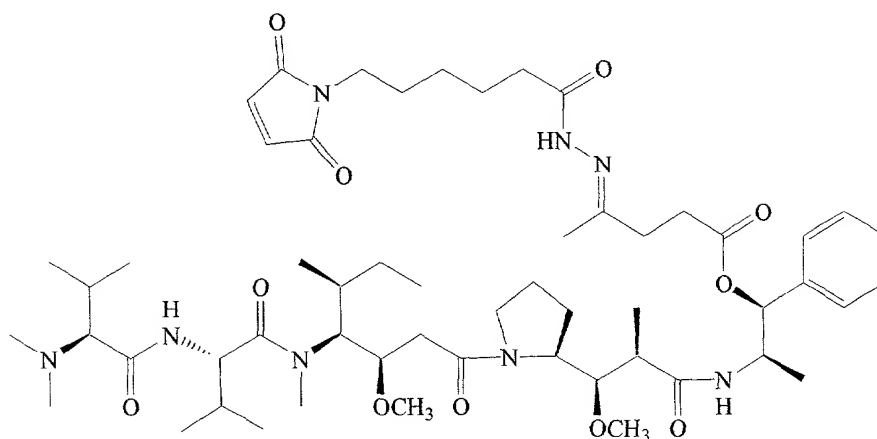
$R^{15}$  is selected from hydrogen, lower alkyl and aryl;

$R^{16}$  is selected from divalent lower alkyl, divalent aryl, and  $-(CH_2OCH_2)_pCH_2-$  where  $p$  is 1-5; and

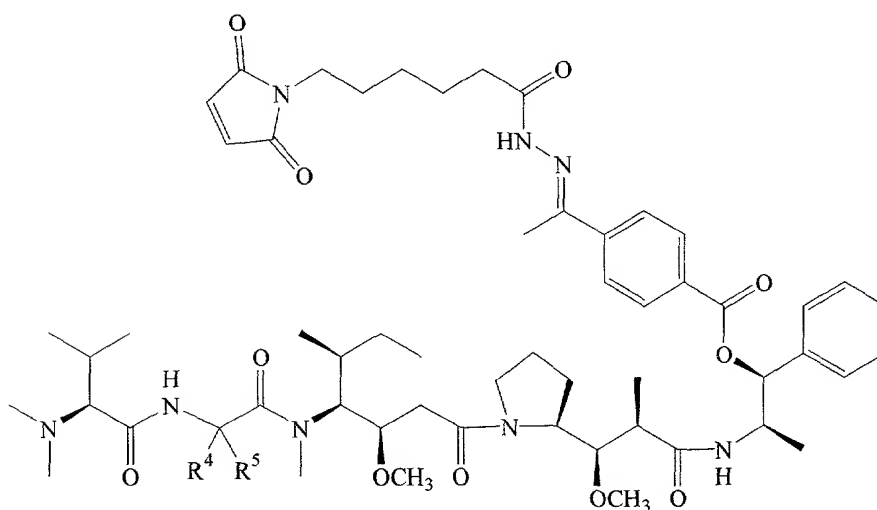


wherein  $X$  is a leaving group.

30. A compound of claim 29 having the formula

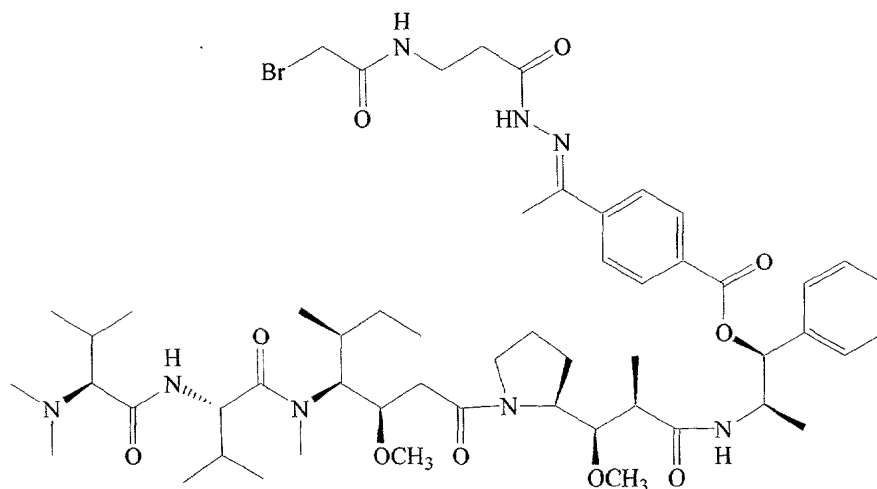


31. A compound of claim 29 having the formula

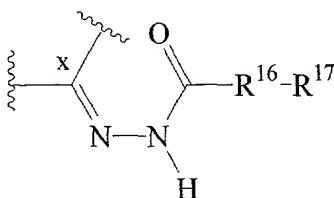


wherein R<sup>4</sup> is selected from *iso*-propyl and *sec*-butyl, and R<sup>5</sup> is hydrogen.

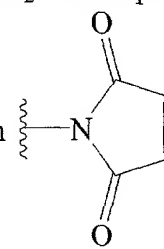
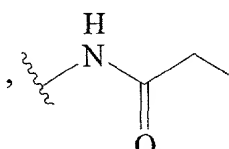
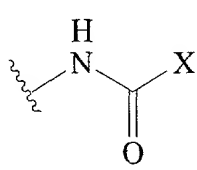
32. A compound of claim 29 having the formula



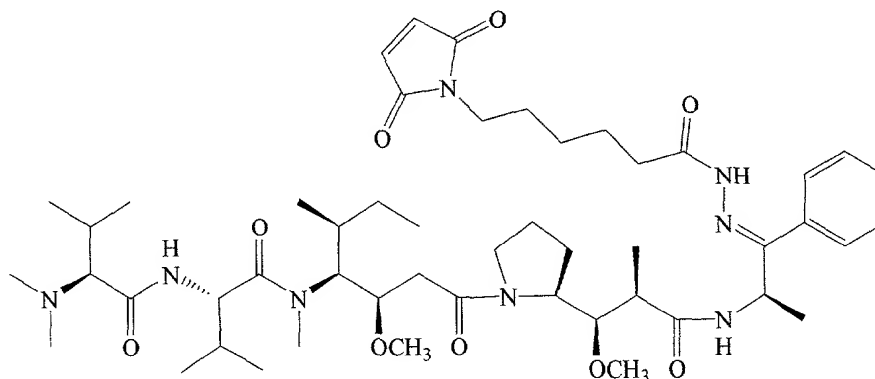
33. A compound of claim 27 wherein  $R^{20}$  comprises a hydrazone of the formula:



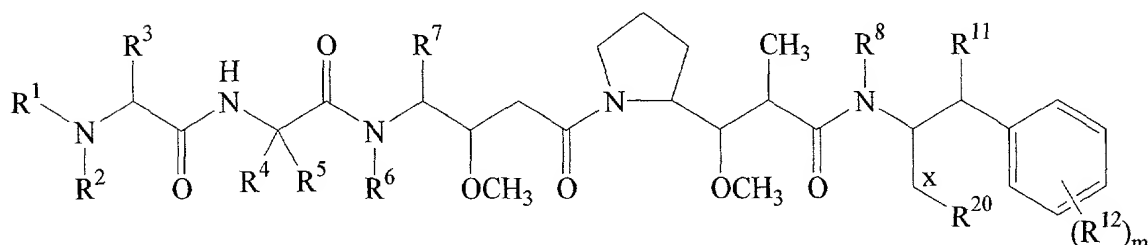
wherein  $R^{16}$  is selected from divalent lower alkyl, divalent aryl, and  $-(CH_2OCH_2)_pCH_2-$  where  $p$  is 1-5, and  $x$  identifies the carbon also marked  $x$  in claim 27; and  $R^{17}$

is selected from , , and  wherein  $X$  is a leaving group.

34. A compound of claim 32 having the formula



35. A compound of the formula



wherein, independently at each location:

$R^1$  is selected from hydrogen and lower alkyl;

$R^2$  is selected from hydrogen and lower alkyl;

$R^3$  is lower alkyl;

$R^4$  is selected from lower alkyl, aryl, and  $-\text{CH}_2\text{-C}_{5-7}\text{carbocycle}$  when  $R^5$  is selected from H and methyl, or  $R^4$  and  $R^5$  together form a carbocycle of the partial formula  $-(\text{CR}^a\text{R}^b)_n-$  wherein  $R^a$  and  $R^b$  are independently selected from hydrogen and lower alkyl and  $n$  is selected from 2, 3, 4, 5 and 6;

$R^6$  is selected from hydrogen and lower alkyl;

$R^7$  is *sec*-butyl or *iso*-butyl;

$R^8$  is selected from hydrogen and lower alkyl;

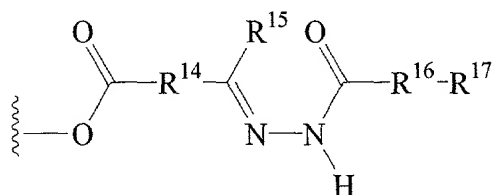
$R^{11}$  is selected from hydrogen and lower alkyl;

$R^{12}$  is selected from lower alkyl, halogen, and methoxy, and  $m$  is 0-5 where  $R^{12}$  is independently selected at each occurrence; and

$R^{20}$  is a reactive linker group having a reactive site that allows  $R^{20}$  to be reacted with a targeting moiety, where  $R^{20}$  can be bonded to the carbon labeled "x" by either a single or double bond.

36. A compound of claim 35 wherein the reactive site is selected from *N*-hydroxysuccinimide ester, *p*-nitrophenyl ester, pentafluorophenyl ester, isothiocyanate, isocyanate, anhydride, acid chloride, and sulfonyl chloride.

37. A compound of claim 35 wherein  $R^{20}$  comprises a hydrazone of the formula

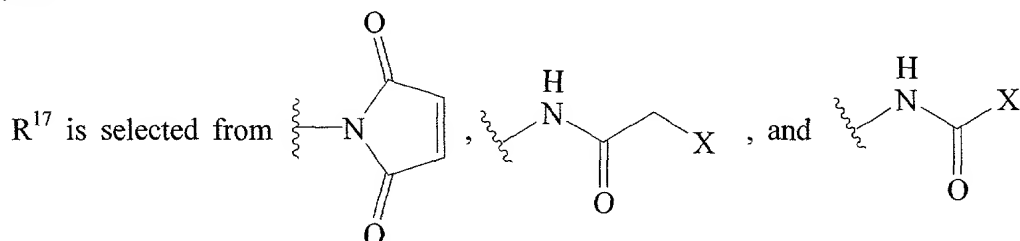


wherein:

$R^{14}$  is selected from a direct bond, divalent lower alkyl and divalent aryl;

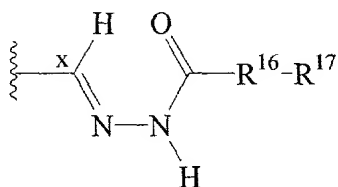
$R^{15}$  is selected from hydrogen, lower alkyl and aryl;

$R^{16}$  is selected from divalent lower alkyl, divalent aryl, and  $-(CH_2OCH_2)_pCH_2-$  where  $p$  is 1-5; and

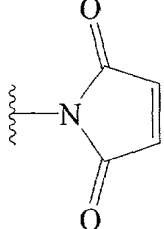
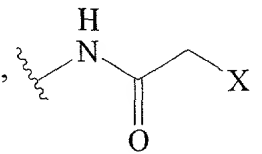
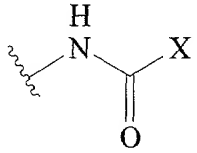


wherein  $X$  is a leaving group.

38. A compound of claim 35 wherein R<sup>20</sup> comprises a hydrazone of the formula:

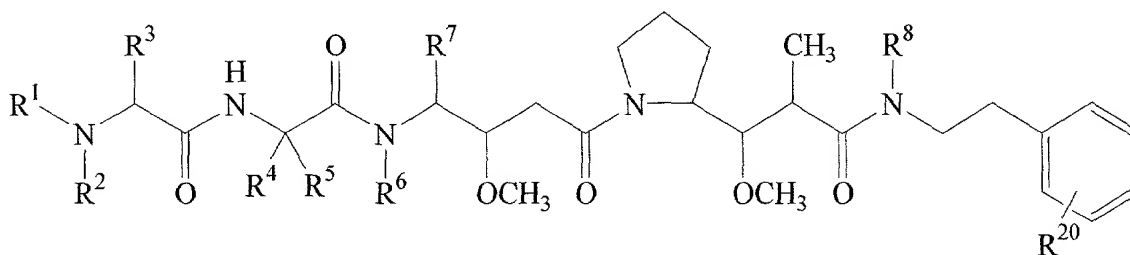


wherein R<sup>16</sup> is selected from divalent lower alkyl, divalent aryl, and  $-(CH_2OCH_2)_pCH_2-$  where p

is 1-5; and R<sup>17</sup> is selected from , , and  where

X is a leaving group.

39. A compound of the formula



wherein, independently at each location:

R<sup>1</sup> is selected from hydrogen and lower alkyl;

R<sup>2</sup> is selected from hydrogen and lower alkyl;

R<sup>3</sup> is lower alkyl;

R<sup>4</sup> is selected from lower alkyl, aryl, and  $-CH_2-C_{5-7}$ carbocycle when R<sup>5</sup> is selected from H and methyl, or R<sup>4</sup> and R<sup>5</sup> together form a carbocycle of the partial formula  $-(CR^aR^b)_n-$  wherein R<sup>a</sup> and R<sup>b</sup> are independently selected from hydrogen and lower alkyl and n is selected from 2, 3, 4, 5 and 6;

R<sup>6</sup> is selected from hydrogen and lower alkyl;

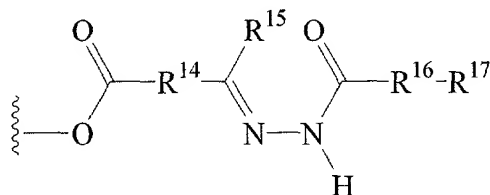
R<sup>7</sup> is *sec*-butyl or *iso*-butyl;

$R^8$  is selected from hydrogen and lower alkyl; and

$R^{20}$  is a reactive linker group comprising a reactive site that allows  $R^{20}$  to be reacted with a targeting moiety.

40. A compound of claim 39 wherein the reactive site is selected from *N*-hydroxysuccinimide ester, *p*-nitrophenyl ester, pentafluorophenyl ester, isothiocyanate, isocyanate, anhydride, acid chloride, and sulfonyl chloride.

41. A compound of claim 39 wherein  $R^{20}$  comprises a hydrazone of the formula

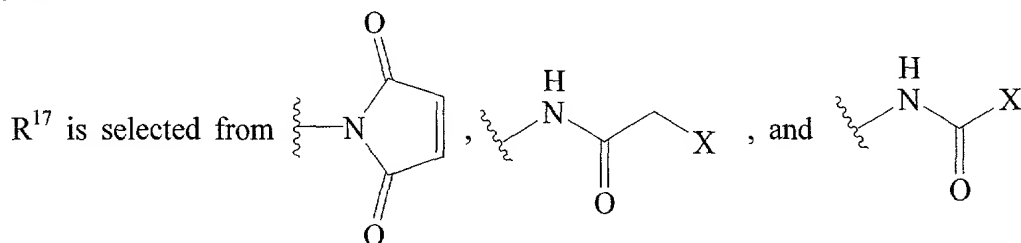


wherein:

$R^{14}$  is selected from a direct bond, divalent lower alkyl and divalent aryl;

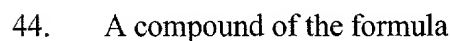
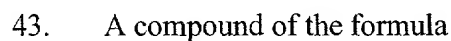
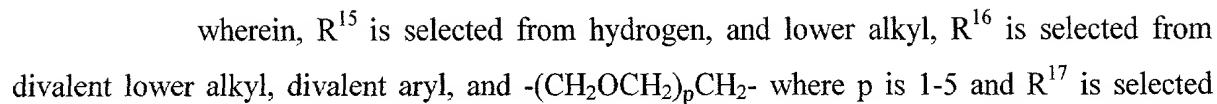
$R^{15}$  is selected from hydrogen, lower alkyl and aryl;

$R^{16}$  is selected from divalent lower alkyl, divalent aryl, and  $-(\text{CH}_2\text{OCH}_2)_p\text{CH}_2-$  where  $p$  is 1-5; and



where  $X$  is a leaving group.

Year	1950	1951	1952	1953	1954	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968	1969	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100																			
Population	1,000,000	1,050,000	1,100,000	1,150,000	1,200,000	1,250,000	1,300,000	1,350,000	1,400,000	1,450,000	1,500,000	1,550,000	1,600,000	1,650,000	1,700,000	1,750,000	1,800,000	1,850,000	1,900,000	1,950,000	2,000,000	2,050,000	2,100,000	2,150,000	2,200,000	2,250,000	2,300,000	2,350,000	2,400,000	2,450,000	2,500,000	2,550,000	2,600,000	2,650,000	2,700,000	2,750,000	2,800,000	2,850,000	2,900,000	2,950,000	3,000,000	3,050,000	3,100,000	3,150,000	3,200,000	3,250,000	3,300,000	3,350,000	3,400,000	3,450,000	3,500,000	3,550,000	3,600,000	3,650,000	3,700,000	3,750,000	3,800,000	3,850,000	3,900,000	3,950,000	4,000,000	4,050,000	4,100,000	4,150,000	4,200,000	4,250,000	4,300,000	4,350,000	4,400,000	4,450,000	4,500,000	4,550,000	4,600,000	4,650,000	4,700,000	4,750,000	4,800,000	4,850,000	4,900,000	4,950,000	5,000,000	5,050,000	5,100,000	5,150,000	5,200,000	5,250,000	5,300,000	5,350,000	5,400,000	5,450,000	5,500,000	5,550,000	5,600,000	5,650,000	5,700,000	5,750,000	5,800,000	5,850,000	5,900,000	5,950,000	6,000,000	6,050,000	6,100,000	6,150,000	6,200,000	6,250,000	6,300,000	6,350,000	6,400,000	6,450,000	6,500,000	6,550,000	6,600,000	6,650,000	6,700,000	6,750,000	6,800,000	6,850,000	6,900,000	6,950,000	7,000,000	7,050,000	7,100,000	7,150,000	7,200,000	7,250,000	7,300,000	7,350,000	7,400,000	7,450,000	7,500,000	7,550,000	7,600,000	7,650,000	7,700,000	7,750,000	7,800,000	7,850,000	7,900,000	7,950,000	8,000,000	8,050,000	8,100,000	8,150,000	8,200,000	8,250,000	8,300,000	8,350,000	8,400,000	8,450,000	8,500,000	8,550,000	8,600,000	8,650,000	8,700,000	8,750,000	8,800,000	8,850,000	8,900,000	8,950,000	9,000,000	9,050,000	9,100,000	9,150,000	9,200,000	9,250,000	9,300,000	9,350,000	9,400,000	9,450,000



R<sup>1</sup> is selected from hydrogen and lower alkyl;

$R^2$  is selected from hydrogen and lower alkyl;



R<sup>3</sup> is lower alkyl;

R<sup>4</sup> is selected from lower alkyl, aryl, and -CH<sub>2</sub>-C<sub>5-7</sub>carbocycle when R<sup>5</sup> is selected from H and methyl, or R<sup>4</sup> and R<sup>5</sup> together form a carbocycle of the partial formula -(CR<sup>a</sup>R<sup>b</sup>)<sub>n</sub>- wherein R<sup>a</sup> and R<sup>b</sup> are independently selected from hydrogen and lower alkyl and n is selected from 2, 3, 4, 5 and 6;

R<sup>6</sup> is selected from hydrogen and lower alkyl;

R<sup>7</sup> is *sec*-butyl or *iso*-butyl;

R<sup>8</sup> is selected from hydrogen and lower alkyl;

R<sup>11</sup> is selected from hydrogen and lower alkyl; and

R<sup>18</sup> is selected from hydrogen, a hydroxyl protecting group, and a direct bond where OR<sup>18</sup> represents =O.

45. A compound of claim 44 wherein R<sup>1</sup> is hydrogen.

46. A compound of claim 44 wherein R<sup>1</sup> and R<sup>2</sup> are methyl.

47. A compound of claim 44 wherein R<sup>3</sup> is isopropyl.

48. A compound of claim 44 wherein R<sup>4</sup> is selected from lower alkyl, aryl, and -CH<sub>2</sub>-C<sub>5-7</sub>carbocycle and R<sup>5</sup> is selected from H and methyl.

49. A compound of claim 44 wherein R<sup>4</sup> is selected from lower alkyl, and R<sup>5</sup> is selected from H and methyl.

50. A compound of claim 44 wherein R<sup>4</sup> and R<sup>5</sup> together form a carbocycle of the partial formula -(CR<sup>a</sup>R<sup>b</sup>)<sub>n</sub>- wherein R<sup>a</sup> and R<sup>b</sup> are independently selected from hydrogen and lower alkyl and n is selected from 2, 3, 4, 5 and 6.

51. A compound of claim 44 wherein R<sup>6</sup> is lower alkyl.

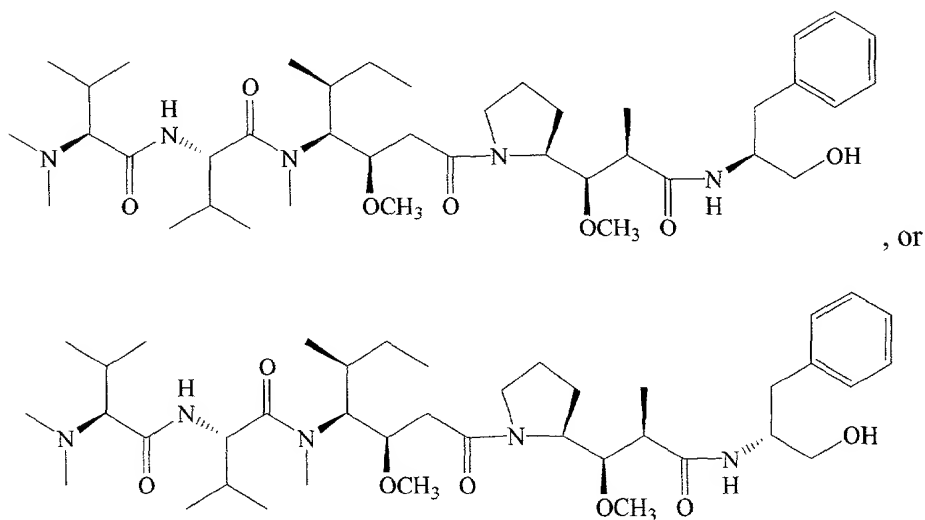
52. A compound of claim 44 wherein  $R^8$  is hydrogen.

53. A compound of claim 44 wherein  $R^{11}$  is hydrogen.

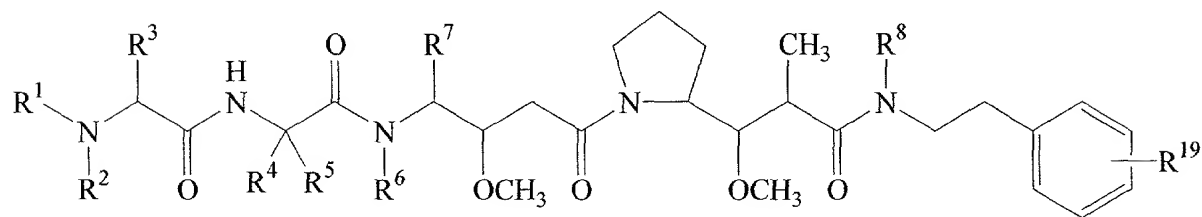
54. A compound of claim 44 wherein  $-OR^{18}$  is  $=O$ .

55. A compound of claim 44 wherein  $R^{18}$  is hydrogen.

56. A compound of claim 44 having the structure



57. A compound of the formula



wherein, independently at each location:

$R^1$  is selected from hydrogen and lower alkyl;

$R^2$  is selected from hydrogen and lower alkyl;

R<sup>3</sup> is lower alkyl;

R<sup>4</sup> is selected from lower alkyl, aryl, and -CH<sub>2</sub>-C<sub>5-7</sub>carbocycle when R<sup>5</sup> is selected from H and methyl, or R<sup>4</sup> and R<sup>5</sup> together form a carbocycle of the partial formula -(CR<sup>a</sup>R<sup>b</sup>)<sub>n</sub>- wherein R<sup>a</sup> and R<sup>b</sup> are independently selected from hydrogen and lower alkyl and n is selected from 2, 3, 4, 5 and 6;

R<sup>6</sup> is selected from hydrogen and lower alkyl;

R<sup>7</sup> is *sec*-butyl or *iso*-butyl;

R<sup>8</sup> is selected from hydrogen and lower alkyl; and

R<sup>19</sup> is selected from hydroxy- and oxo-substituted lower alkyl.

58. A compound of claim 57 wherein R<sup>1</sup> is hydrogen.

59. A compound of claim 57 wherein R<sup>1</sup> and R<sup>2</sup> are methyl.

60. A compound of claim 57 wherein R<sup>3</sup> is *iso*-propyl.

61. A compound of claim 57 wherein R<sup>4</sup> is selected from lower alkyl, aryl, and -CH<sub>2</sub>-C<sub>5-7</sub>carbocycle and R<sup>5</sup> is selected from H and methyl.

62. A compound of claim 57 wherein R<sup>4</sup> is selected from lower alkyl, and R<sup>5</sup> is selected from H and methyl.

63. A compound of claim 57 wherein R<sup>4</sup> and R<sup>5</sup> together form a carbocycle of the partial formula -(CR<sup>a</sup>R<sup>b</sup>)<sub>n</sub>- wherein R<sup>a</sup> and R<sup>b</sup> are independently selected from hydrogen and lower alkyl and n is selected from 2, 3, 4, 5 and 6.

64. A compound of claim 57 wherein R<sup>6</sup> is lower alkyl.

65. A compound of claim 57 wherein R<sup>8</sup> is hydrogen.



- a. delivering a compound of any one of claims 43-67 to a cell, where the compound enters the cell;
- b. cleaving mAb from the remainder of the compound; and
- c. killing the cell with the remainder of the compound.

74. A method of killing or inhibiting the multiplication of tumor cells or cancer cells in a human or other animal, the method comprising administering to the human or animal a therapeutically effective amount of a compound of any one of claims 1-26.

75. A method of killing or inhibiting the multiplication of tumor cells or cancer cells in a human or other animal, the method comprising administering to the human or animal a therapeutically effective amount of a compound of any one of claims 43-67.